

Application No. 10/699,393  
Response Dated January 18, 2007  
Second Reply to Office Action of August 24, 2006

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### Amendments to the Claims

This listing of claims will replace all prior version and listings of claims in the application:

### Listing of Claims:

1. (Currently amended): A protein comprising variant thrombin comprising an amino acid sequence having the substitutions W215A and E217A, wherein the variant thrombin amino acid sequence is at least 80% identical to the sequence set forth [[in]] by SEQ ID NO: 3 and has the substitutions W215A and E217A, and wherein the variant thrombin has a PA/FC ratio greater than 1.0.
2. (Currently amended): The variant thrombin according to protein of claim 1, wherein the variant thrombin comprises comprising a the thrombin B-chain comprising the amino acid sequence as set forth [[in]] by SEQ ID NO: 4.
3. (Withdrawn): The variant thrombin according to claim 1, wherein the variant thrombin is encoded by a nucleic acid comprising the sequence as set forth in SEQ ID NO: 5, or a degenerate variant thereof.
4. (Withdrawn): The variant thrombin according to claim 2, wherein the variant thrombin is encoded by a nucleic acid comprising the sequence as set forth in SEQ ID NO: 6, or a degenerate variant thereof.
5. (Canceled).
6. (Currently amended): The variant thrombin according to protein of claim 1, wherein the variant thrombin has having a PA/FC ratio greater than 150.

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7. (Currently amended): The ~~variant thrombin according to~~ protein of claim 1, wherein the ~~variant thrombin~~ protein is expressed from a recombinant nucleic acid within a cell.
8. (Withdrawn): The variant thrombin according to claim 7, wherein the recombinant nucleic acid comprises a sequence selected from SEQ ID NO: 5 and SEQ ID NO: 6, or a degenerate variant thereof.
9. (Withdrawn): A nucleic acid encoding a variant thrombin and comprising a nucleic acid selected from SEQ ID NO: 5 and SEQ ID NO: 6, or a degenerate variant thereof.
10. (Withdrawn): The nucleic acid according to claim 9, wherein the nucleic acid is in an expression cassette.
11. (Withdrawn): The nucleic acid according to claim 10, wherein the expression cassette is in a vector.
12. (Withdrawn): A cell having a nucleic acid comprising the sequence selected from SEQ ID NO: 5 and SEQ ID NO: 6, or a degenerate variant thereof, and capable of producing a variant thrombin protein according to claim 9.
13. (Withdrawn): A physiologically acceptable composition comprising:
  - (a) a variant thrombin, wherein the variant prothrombin has the amino acid substitution W215A and is at least 80% identical to the amino acid sequence as set forth in SEQ ID NO: 1; and
  - (b) at least one pharmaceutically acceptable carrier.
14. (Withdrawn): The physiologically acceptable composition according to claim 13, wherein the variant thrombin comprises the amino acid sequence set forth in SEQ ID NO: 1.

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15. (Withdrawn): The physiologically acceptable composition according to claim 13, wherein the variant thrombin comprises the amino acid sequence set forth in SEQ ID NO: 2.
16. (Currently amended): A physiologically acceptable composition comprising:
  - (a) ~~a variant thrombin, wherein the variant prothrombin has the amino acid substitutions W215A and E217A, and is at least 80% identical to the amino acid sequence as set forth in SEQ ID NO: 3~~the protein of claim 1; and
  - (b) at least one pharmaceutically acceptable carrier.
17. (Original): The physiologically acceptable composition according to claim 16, wherein the variant thrombin has the amino acid substitutions W215A and E217A, and comprises the amino acid sequence set forth in SEQ ID NO: 3.
18. (Original): The physiologically acceptable composition according to claim 16, wherein the variant thrombin has the amino acid substitutions W215A and E217A, and comprises the amino acid sequence set forth in SEQ ID NO: 4.
19. (Withdrawn): A method of inhibiting the formation of a thrombus, comprising the steps of:
  - (a) delivering to the blood of an animal or human a physiologically acceptable composition comprising an effective amount of a variant thrombin with substantially reduced procoagulant activity, wherein the variant thrombin has the amino acid substitution W215A and comprises an amino acid sequence at least 80% -identical to the amino acid sequence set forth in SEQ ID NO: 1; and
  - (b) allowing the variant thrombin to activate protein C, thereby inhibiting thrombus formation.
20. (Withdrawn): The method according to claim 19, further comprising the step of administering to the animal or human a variant prothrombin capable of being converted to the variant thrombin.